

Fig. 1A-1C

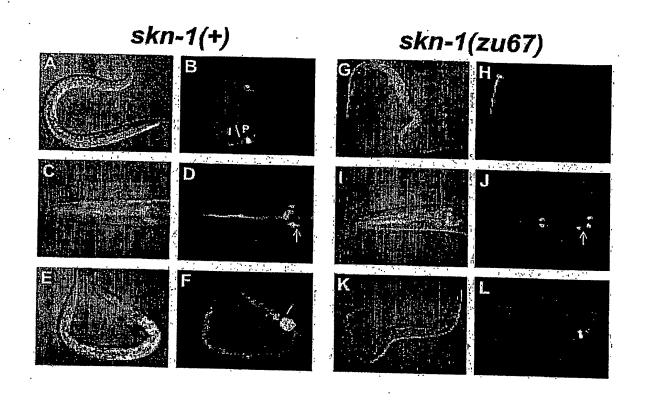


Fig. 2A-2L

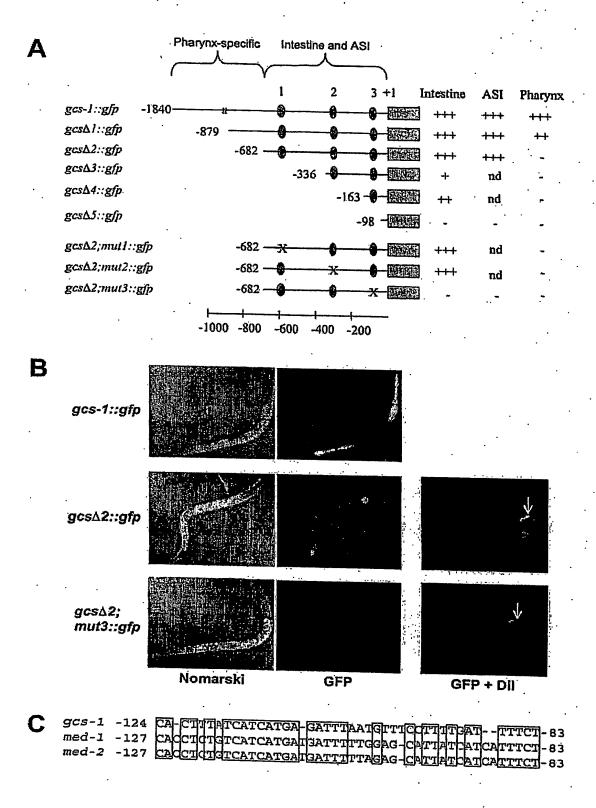
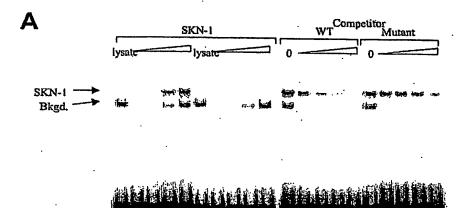
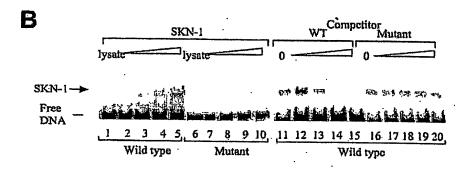


Fig. 3A-3C





Mutant

Wild type

Wild type

Fig. 4A-4B

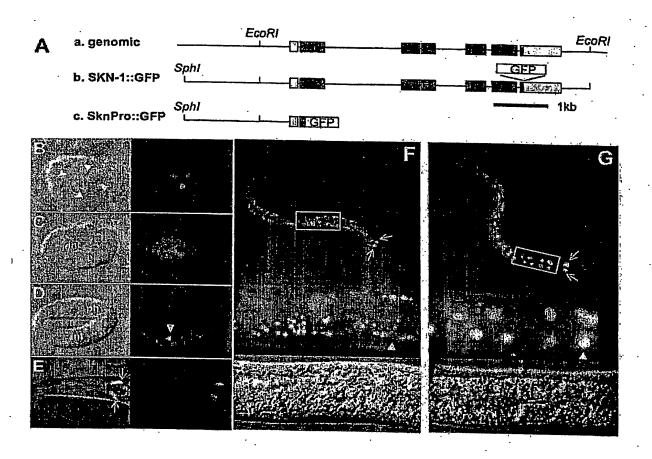
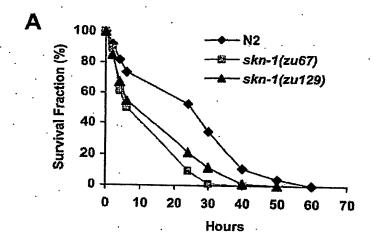


Fig. 5A-5G



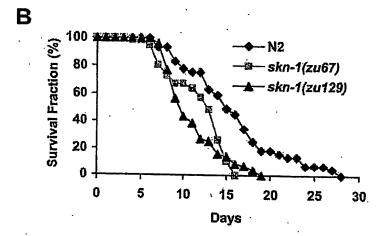
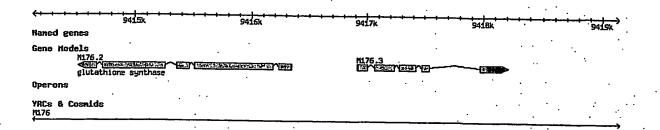


Fig. 6A-6B



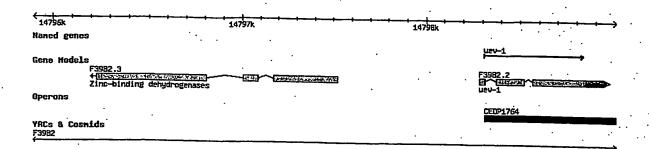
The M176.2 gene is located on chromosome II. Regulatory sequences can be found e.g., in the region between 9416340 and 9415915. An exemplary sequence of this region is as follows:

 $\hbox{\tt CATAGAAACCTCACGTTATACGT}{\hbox{\tt TTTGTCAT}} \hbox{\tt CACGATTTCAGTGCTCACTTTCTCATTCATTCTCGCT}{\hbox{\tt -137}}$ 

#### Exemplary M176.1 sequences:

			Amino Ac	ld Sequen	e e			7
MWÖKDDKTTT	<b>PUMBERTED</b>	DKLNELTADL	HDWAHANGLV	MRLSTDKLSS	EVCOTTOT.TT.	TDCDCDCATCC	DDB1007-00	đ
MGAHALKLIE	MHIKATKATN	ISDDVIORAL	PENKPIPMIA	EALFKAWSHE	CNDAMMINA	VENUMONOTO	QIEINNIASS QRHVEYELEK	
TGABULCTIK	KNTLOCAROP	SLNDRSDLMI	DGROVAIVYF	RAGYSPDHYP	STREWEADED	METCHATION	WIGLQVANTK GDEMVOMLRE	
LPEEERGAFI VDTPFLYEFI	TWEKTKЪWII	ENYLVLAKKP	ITFAKAVSEL	GVYGYAFGRK	DAPELKTAGH	LLRTKPESTA	GDEMVQMLRE MGGVAAGHAV	
VDIFFDIEFI			•					

#### Spliced mRNA aaagaATGGCT CAAAAAGATG ACCGGATTTT GCTGTTGAAT GCTCCAAGGC TCCCGCTCGA AGATGATAAG CTCAACGAGC TCACCGCTGA TCTTCACGAT TGGGCTCATG CTAATGGGCT TGTCATGCGT CTATCAACCG ACAAGTTGAG CAGCGAAGTT TGTCAAACTA CTCCATTAAC ACTTCTTCCA TCTCCATTCC CGAAAAATGT TTTTGAAGAA GCAGTTCATA TTCAGAACCT TTTCGCAAGT CTTTATCACT TCATAGCTTA TGAATTTGAT TTTCTAATCG ATATTCATAA AAATGTCGTG AAAACTGATG ATTTCACACG GAATATGGTT GAGATCTTGA AGAAAGTCAA AGCCCAAGGA CTCAAGCAAC CAGTCACTCT CGCGATTCAA CGATCTGATT ATATGTGTCA TAAGGATCAA TATTCAGCGG AATATGGACT GAAACAAATT GAAATAAACA ATATCGCCTC GTCAATGGGA GCACATGCTC TACGGCTCAC CGAATGGCAT ATCAGAGGTTC TTAAAGCGTT GAACATTTCC GATGACGTCA TTCAAAGAGC AATTCCAGAA AACAAGCCAA TTCCAATGAT CGCTGAAGCT TTATTCAAGG CCTGGTCCCA CTTTTCGAAC CCAGCAGCTG TGGTTCTTGT CGTTGTAGAA AACGTCAATC AAAATCAGAT TGATCAACGC CACGTGGAAT ATGAACTTGA AAAGTTAGGA GTACCGATGA CATGTATTAT TAGAAGAAAT TTAACACAAT GCTATGAACA ATTATCATTG AATGATAGAA GCGATTTGAT GATTGATGGG CGTCAAGTAG CAATTGTTTA CTTCAGAGCA GGATACTCAC CTGATCATTA TCCATCTACA AAAGAATGGG AAGCACGTGA GCGTATGGAA CTTTCCACCG CTATCAAAAC TCCATGGATC GGGCTACAGG TGGCAAATAC TAAGAAGACC CAGCAGGTTC TTTCTGAAGA TGGAGTACTC GAAAGATTCA TCGGAAAACC ACGAGAAGCT CGCGATATTC GAGCTTCATT CGCAGGAATG TGGGCTTTGG AGAACACTGA TGAAGTGACT ATGAAAGTCG TGGCTGGAGC TCAAAAACAT CCAGAAGCGT TTGTTCTGAA GCCACAAACT GAAGGTGGAG CCGCATTGCA CACCGGTGAT GAGATGGTTC AAATGCTCCG AGAACTTCCG GAAGAAGAGC GTGGAGCTTT CATTTTGATG GAGAAACTGA AACCGATGAT TATTGAAAAC TACCTGGTTC TTGCAAAGAA GCCGATCACA TTTGCTAAGG CTGTTAGTGA ACTTGGAGTG TATGGTTATG CATTTGGAAG GAAGGATGCA CCTGAGCTTA AGACTGCTGG GCATTTGCTC CGAACGAAAC CGGAATCCAC AGCTATGGGT GGAGTAGCCG CCGGACATGC TGTTGTCGAC ACCCCATTCC TCTACGAATT TATTTGAttt cgaacataat cagaaaactc aacaaaaatg ctgtgatatg aaaccatttg ctatttagat ctttttgtgt ttgtaaattt aatcattgta atttattgaa tgt



The F39B2.3 gene is located on chromosome I. Regulatory sequences can be found e.g., in the region between 14 797 521 and 14 798 310. An exemplary sequence of this region is as follows:

 $\begin{tabular}{l} CATTTTGAAAGTGCCCAAGTTGCTGGAACGCTGAAAATTGAAATTATTAACAAAGAAATTTGCTTTAAAA\\ TCCGAAAAATCAAGAAAAATCGATAATTTCGTCGGACAATCCGCCTGCTAGCACGGCTTGACGCTCGTT\\ TGCCGCGCGCTCATTCGATTTGTGTGAGTGCCCAGTGGAGCGCGTTTGCTAAGGCTAACTGTGTAGTCCT\\ CTCGGACAAGATCTGTGAACATTGAAATGAAACACTTGGGTTCAATAAAATCACAAGAAAATGATGACAA\\ \hline -518 \end{tabular}$ 

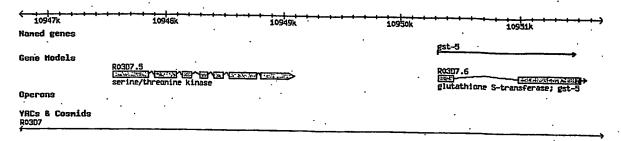
TTTTGTTTGCGACCGAAAAAAATTATAAAAATTGAATATTGGTTATCATCGTTTCAATCTTTGTTTTGT

## 10/39

## Exemplary F39B2.3 sequences:

Amino Acid Sequence  MSKSICKSSM RAAVVRFGA PDVIEAVESD MPRLEKNOVL VRNYAAGVNP VDTYIRAGQY GKLE VGESVKNVKV GDRVWYGSEA DSTAEYVAVN RPFELPEGVS FEEGASLGVP YLTAYRALFH LAGA SALMQLAAWR NIEAVGTAGS ADGIRFVKSL GARNVYNHSD KQYVSKMKND YPGGFNHIFE MAAH AVIGNRAETT INARQLMVTE GAVYGVALGM SSEAELLDFG INIVSFLKET EFRPLINKLY RLEQ	PNLPYVP GKDGAGFVEL AKTGDVI LVHGASGGVG
MLVVQIER	

			Shire	J. H. DRIA				Š
								ă.
ATGAGCAAAT	CONTITIONN	MICAMGCATG	CGCGCAGCTG	TACTCCCACC	$\Delta \Pi \Pi$	0000		ď
	11100001000	TIGORAMA	CCAGGTTCTC	Carrer Carab Arrer	ACCCMCCCC	momes		
111111100100	TOGIOUGIAI	GGMMMCIAC	CAAATCTTCC	ΑΨΑΨΩΨΑΥΛΆ	<b>CCNNNNCNM</b> C	030000		
	COCTTTTTTT	TOTOWNYGIC	GGCGATCGAG	TCTGGTATCG	<b>ልጥሮ</b> እርከ አሮሮሮ	CACACERO		
70000707777	CONCOURTICG	MODIFICA	AGGAGTTTCG	THICACCIANC	CACCMMomom			
	111 1011 1011	CITOCIGGIC	CAAAISAI "ITSIS	CCACCOUNTAIN		~~~~		
	**********	TOCCIOCAGG	AACATTGAAG	CHIGHINGGCAAC.	m	00000		
	001001100011	WIGICINIAN.	TCATTCGGAT	AAGCAAGAG	中に中にとれ カカカm	~~~~~~		
	Ot 11 T T T O O O 1 T J	TI GGCIGCIC	ACACAAATCT	GAACACCAC	CmCCCMmmcc	Maaaaaa		
COLIGITATIO	GUTUT COCOC	CGAGACCACG	ATCAACGCAA	CACAACTTAT	ここがかり へんてん カ	CC3 CC5		
	10110000000	CIGUGCICII	GGACTTTGGG	ATICAACATTIC	$m_{C}m_{C}$ $m_{C}m_{C}$	C3 3 CC5		
OTTO T TTTTTTT	CULTITION	CGICICGAGC	AATTAGGACT	CCCTCATCAC	CNDNMMAKAN	ACAACAAGGG	GAGTTTCGTC	
AATCTTGTAG	TGCAAATCGA	ACATTAAttc	attattttaa	caccccattt	aaaaaaa	TOTAL MAGGG	AGCGAAAGGA	
				3	-uugguu			



The R03D7.6 gene is located on chromosome II. Regulatory sequences can be found e.g., in the region between 10949088 and 10950317. An exemplary sequence of this region is as follows:

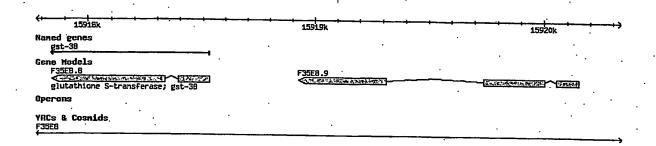
-947

## 

ACTGAATTCTCTTTCCGAAAGACCACCACAATTTCAGGGCTCCGCCCATTTCGTGGTTTGTAGCCTTCCCGACCCTACGT
TTTTGATGACAATTGTGAGAGAGAGAGAGGTTCAGACACAAAAAGCGACGTGGTCGAATGA
-149

## Exemplary R03D7.6 (gst-5) sequences:

MVSYKLTYFN GRGAGEVSRQ GKTAWEEAQV NSLADQYKDY AIAQHSADLI AKGGDFSKFP	SSEARPYFYA IMGEGDODI	P ALKETCAAPF GQI	LPFLEVDG KKLAQSH	IAIA RFLAREFKLN GFL VGDSLTWIDL
CATTCCTCGA AGTCGACGGT GGAAAAACCG CCTGGGAAGA TTTCTACGCT GTCATGGGAT	AAGAAGCTTG CTCAATCCC GGCTCAAGTG AACTCTCTT TCGGTCCAGG AGACGTTGA TTCTTGAAGG CTTCGGGAT	G CTGGAGAAGT GTC A GCATTGAAAG AAA A CGCGATTGCT CGT G CCGATCAATA CAA A ACTTTGAAGA AAG C CGGATTCCTT GTC	CTCGTCAG ATTTTCG ACCTGCGC TGCTCCA TTTCTTGG CTCGTGA AGGATTAT TCAAGTG EACATCTT CCTTCCA CGGAGACT CTTTGAC	CCT ATGCCGGACA TTC GGACAACTTC GTT CAAGCTCAAC AGG CTCGTCCATA GCA TTTGAAAAGT CTG GATTGACTTC



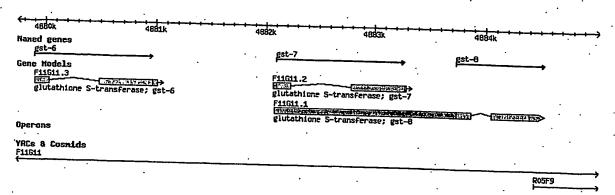
The F35E8.8 gene is located on chromosome V. Regulatory sequences can be found e.g., in the region between 15 917 841 and 15 918 925. An exemplary sequence from in or around this region is as follows:

GATTCTCAACGGTTTATTTTCTGTCACAACTCTTCCTAATATTCACCATGGTTT

## Exemplary F35E8.8 (gst-38) sequences:

	Amino A	id Sequence	
MASIVILLE CKCACETCKO	YAEARPYLAV KLGYTEGDAR	KFKAAGKTPY NOLPMLEVDO	KPLAQSHAMA RYLAREFGFN ALKASGSGFL VGNSLTFIDL

			e Solice	omrna.			
GAAATATGAA CAATGCTCGA GGAAAGAGCA CCTCGCTGTG ACTATGGATT CTTGTTGCTC	GATAACAGAC GGTAGATGGC GATGGGAAGA AAGCTTGGTT CTTTGTCAAT AGCATTCAGC	TTACCGATGA AAACCACTCG AGCTCAAGTC ACACAGAAGG GCTTTGAAGG TGATTTGCTG	GGACGCGGAG GGAGTGGGAG CTCAGTCCCA AACTCCTTGG AGACGCGGAG CCAGCGGGTC GGACGTGAAA	CCGGAGAGCT AAGTTCAAAG CGCGATGGCT CCGACCAGTA GCTCTTTACA AGGATTCTTG	CTGCCGTCAA CGGCCGGAAA CGTTATCTTG CAAAGACTAT CAAGCGTCTA GTTGGAAATT	ATCTTTGCTG AACCCCATAC CTCGGGAATT TACGCGCAGG TCTTCCAGTT CCTTGACTTT	CCGCCGAGCA AACCAGCTTC CGGGTTCAAC CTCGTCCATA TTCAAGAAAC TATTGATTTG
TTCCGAAAAA	GTTCAGTCAA	TTCCTCAGAT	CAAGAAATGG	ATTGAGACTC	GTCCAGCGAG	TGACTGGTAA	



The F11G11.2 gene is located on chromosome I. Regulatory sequences can be found e.g., in the region between 4 880 968 and 4 882 068. An exemplary sequence in or around this region is as follows:

AAGATGATTGATGCCATGGGTTTATATTTGTGAGTAGTCACAAATTGTGACACAACATTCCCTTCGAAAGATCTGGAAAA
GTCACAAAACCTTGCATATATTTTTTTCAACCAATATTATTTTTGACCTACTCTGTTCATCGTAACATTGCAACAAAA
AACGATGACTACACTTTATGATTTCTAGTCAACAACGTGCGCGCAATGTGTAGAGCAAATGATGACAAAACTACAGAATAT
GGTGAGTGGAGAGACACAGACATTTGAGAAATGGGTATAAATA
-133

## Exemplary F11G11.2 (gst-7) sequences:

#### Amilio Acid Seguence

MVHYKVSYFP IRGAGEIARQ ILAYAGQDFE DNRIPKEEWP AVKPSTPFGQ LPLLEVDGKV LAQSHAIARY LARQFGINGK CAWEEAQVNS VADQFKDYLN EVRPYFMVKM GFAEGDLDAL AKDVFLPGFK KHYGFFANFL KSAGSGYLVG DSLTFVDLLV AQHTADLLAA NAALLDEFPQ FKAHQEKVHS NANIKKWLET RPVTPF

#### SplicedimRNA

CGACCACTCG
AGATTCTC
AAGCCAAGCA
TTACTTGGCT
GCTCAGTTCG
GCAATCAATC
GCAATCAATC
GCAATCAATC
GCAATCAATC
GAATCAATC
GAAGAATC
TTACAGAATC
TTCCAGGATT
TTCCAGGATT
TTCCAGGATC
TTCAAGAACC
TTGACCTTC
TTCCAGGATC
TTGACCTTC
TTGACCTC
AAAAGGATC
TTTGCAAGTC
TTTGCAAGTC
TTTGCCAAGCA
TTTGCCAAGCA
TTTCTAACT
TTGCCAACCC
TTGCCAACCC
TTCCAAGTC
TTGCCAACCC
TTCCAAGTC
TTGCCAACCC
TTCCAACTC
TTGCCAACCC
TTCCAACTC
TTCCAACTC
TTCCAACTC
TTCCAACTC
TTCCAACTC
TTCCAACTC
TTCCAACTC
TTCCAACTC
TTCCCAACCC
TTCCCACCC
TTCCCACCC
TTCCCACCC
TTCCACCC
TTCCACC

The K08F4.7 gene is located on chromosome IV. Regulatory sequences can be found e.g., in the region between about 10141800 and 10142217. An exemplary sequence of this region is as follows:

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 ${\tt TCCACGATTTACACTCTCAAGTGAAACCAACTGTTCTTTGATGCCAGACG\underline{{\tt ATGACATT}{\tt ACACTTGATAAGA}}$ 

AAATATATAAAACTGGAATTAAAAACAATTGATACATCGATTCAATTACTGAATTCTAATT**ATG** 

## Exemplary K08F4.7 (gst-4) sequences:

#### Amino Acid Secuence

MPNYKLLYFD ARALAEPIRI MFAMLNVPYE DYRVSVEEWS KLKPTTPFGQ LPILQVDGEQ FGQSMSITRY LARKFGLAGK TAEEEAYADS IVDQYRDFIF FFRQFTSSVF YGSDADHINK VRFEVVEPAR DDFLAIINKF LAKSKSGFLV GDSLTWADIV IADNLTSLLK NGFLDFNKEK KLEEFYNKIH SIPEIKNYVA TRKDSIV

#### Spliced mRNA

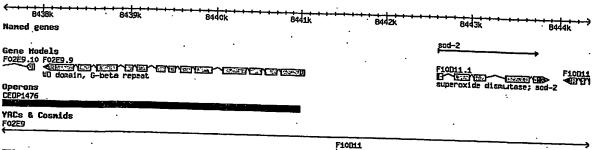
The sod-1 gene is located on chromosome II. Regulatory sequences can be found e.g., in the region between about 6 973 806 and about 6 974 406. An exemplary sequence of this region is as follows:

TTATTATTCAAAGTTGTAGATTCAGTATTTTAGATCGGTGATG

#### Exemplary sod-1 sequences:

MFMNLLTQVS NAIFPQVEAA QKMSNRAVAV LRGETVTGTI WITQKSENDQ AVIEGEIKGL TPGLHGFHVH QYGDSTNGCI SAGPHFNPFG KTHGGPKSEI RHVGDLGNVE AGADGVAKIK LTDTLVTLYG PNTVVGRSMV VHAGQDDLGE GVGDKAEESK KTGNAGARAA CGVIALAAPO

tttagatcgg tgATGTTTAT GAATCTTCTC ACTCAGGTCT CCAACGCGAT TTTTCCGCAG GTCGAAGCCG CTCAAAAAAT GTCGAACCGT GCTGTCGCTG TTCTTCGTGG AGAAACTGTT ACCGGTACTA TCTGGATCAC ACAGAAGTCC GAAAATGACC AGGCAGTTAT TGAAGGAGAA ATCAAGGGAC TTACTCCCGG TCTTCATGGA TTCCACGTTC ACCAATATGG TGATTCCACC AACGGATGCA TTTCTGCCGG TCCACACTTC AATCCATTTG GAAAGACTCA TGGTGGACCA AAATCCGAGA TCCGTCACGT AGGCGATCTA GGAAATGTGG AAGCTGGAGC CGATGGAGTG GCAAAAATCA AGCTCACCGA CACGCTCGTC ACGCTTTACG
GTCCAAACAC TGTCGTTGGC CGATCTATGG TTGTTCATGC CGGACAAGAC GACCTCGGCG AGGGAGTCGG AGACAAGGCA
GAAGAGTCCA AGAAGACTGG AAACGCCGGA GCTCGTGCTG CCTGCGGTGT CATTGCTCTC GCTGCTCCCC AGTGACCACC tgaatcgcgt ctctgaatct ccacacaatt cctactaaag acaatttttc atttcttgct ttgtcgttat attcttaaga atcccgttgt tcctactcct actactgtat attttcacat aaaatttctt caaaatttca aataaaggtt gtagtttc



The sod-2 gene is located on chromosome I. Regulatory sequences can be found e.g., in the region between about 8 441 038 and 8 442 612. An exemplary sequence of this region is as follows:

GTGCTACCAGCTCTCCTGTATGCTAGTGAAACTTGGACTTGTAATGCTGGATCCACGTTGAGACTCAAAAGAACTGTCAC
CGGTCTCATCGACGCTGCAGAAATTCGAGGCTGGAACTTCAACTTGGAACGTTACCTCCTTGCAAAACAATCAAGATTTG
CAGGACACATTCTACGGAGAGATCCAAACCGATGGACAAAAATCTGCACGGAATGGGACCCGAGCCACAACAAAAATTGG
AAACGTGCCGTTGGAGGACAGAAGAAGAAGAGGCTAAGGACATCGACGAAGAATACGCAAAAATTCCGC
CATGTCGGGACAAGTCGTTGTTGGGAGAAGAAGACTAGGAATGCTCACTCCGAAGGCTCCATGGCTGTCCATCGCACGAA
CCGACCGTGAAAAATGGAAAAGAGTTTGTCCGCAGTTGCCTCGCAACTTGAACCCAACGGACATCAAAGTATCAAAGTAAG
TAAGTAAGTAACCTGAATAAAAAACGTTGCAATTAAAAAATCTACTCGAAAATTAAGTGAGAATTGAAGGATTGCTT
TCCGAAGAGAAAATGACAATTATAGGGTATACTAAAAACATCAAAAATGTATATTAGACTACCATAAATATTACGATAAT

TTAAAAATTACTAGAAACACGCAATTCGGCTCAAAAAGCAACAATTTAGACTGAAAACGAGCTAAAAGAATATTATTCAA
AAACCACTTTGCTCGGTAAATCTGG<u>TGTATCAT</u>GTTCCGCAAACACTGTCTTTTGTTTTGCG

-1 01

## Exemplary sod-2 sequences:

MLQNTVRCVS KLVQPITGVA AVRSKHSLPD LPYDYADLEP VISHEIMQLH HQKHHATYVN NLNQIEEKLH AIALQPALKF NGGGHINHSI FWTNLAKDGG EPSAELLTAI KSDFGSLDNL QKQLSASTVA VQGSGWGWLG ATCANQDPLE ATTGLVPLFG IDVWEHAYYL QYKNVRPDYV NAIWKIANWK NVSERFAKAQ Q	EAVSKGNVKE YCPKGKILKV
tttgcagccg aaaATGCTTC AAAACACCGT TCGCTGTGTC TCAAAGCTTG TTCAACCGAT CACAGGAGTC GCTCGAAGCA AGCATCATCAA AGCATCATCAA AGCATCATCAA AGCATCATCAA AGCATCATCAA GCACTATGC CTCTTCAGCC AGCTCTCAAG CTCAAAAACACGTC AAAAGAACCGTAA AAAAACACGTCAA AGCATTATGG GGAAAACCATC CTCTTCAGCC AGCTCTCAAG GAAACCATATC CTCTCAGCC AAAAAAACACGTCAA AGCATTCGGAACCACTC CGCGGAGTT GCTCAAGAAAAC AGCTTTCGGC ATCAACTGTC GCTGTCAAG GATCAGGATG GGGATAGTTG GCTCAAGAAACA GTGCCAATCA GGATCCACTT GAGGCAACAA CTGGACTTGT TCCACTGTTC TCGGGAGCA AGAACCATC CGCTTACTAC GTGCCAATCA AGAATGTTC GAGGCAACAA CTGGACTTGT TCCACTGTTC ACCAGTTAT GTCAATGCTA TTGCAGTACA AGAATGTTC ACCAGTTAT GTCAATGCTA TTTGGAAGAT AGAACGTCA AGAACGTCA ACCAGTTAT GTCAATGCTA TTTGGAAGAT AGAACGTCA ACCAGTTAT GCAAAGGCA CAGCAATAAA tgagctgaat cacaagaatt aatcgtcaaa aatcgtcaaa ttttgtttct aaattattcg aaatgtaaat tttcaaacct tttgtttct	TATGCAACTT TCTCCAAAGG ATCTTCTGGA TCTGGATAAT CAAAGGGAAA GGAATTGACG CGCCAACTGG

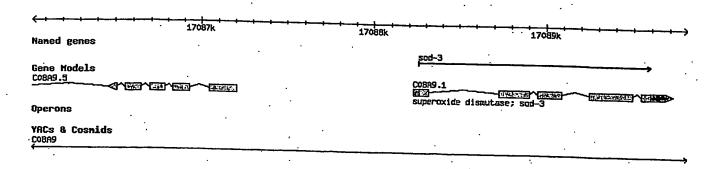
FIG. 22

The ctl-1 gene is located on chromosome II. Regulatory sequences can be found e.g., in the region near 14 306 135. An exemplary sequence of this region is as follows:

GCACCGCGACTGGGAGTATAAGAATCGCCGGAAAACATCAATAATCAGTTCGGTAGAAGTGAAAATTGAG CGTAAAAT<u>ATGATCAT</u>TTTTCGATGCACCATATTTGACGCGCAATACTTCTACAAGCCGCTGTGTACTGC -880

## Exemplary ctl-1 sequences:

					id Sequen	Market 187 - 1882 CMD - 25 MARK			
	IHALKRNPQT. LDPTDAGKLA YFAEVEQAAF	HMRDPNALFD SSDPDYAIRD CPAHIVPGIE DDVKESTFQT	FWMNRPESIH LFNAIESRNF FSPDKMLOGR	QVMFLYSDRG PEWKMFIQVM IFSYTDTHYH	TVRDPRGFSL IPDGFRFMNG TFEQAEKWEF	YGAHTFKMVN NPFDVTKVWP	DRERIPERVV LVGNNTPIFF KEGNPIYCKF HGDYPLIEVG TTQRDGAMAY DLGGCLEEIQ	IRDAIHFPNF HFKPAQGSKN KMVLNRNVKN	1
				. eo	veline:				
•	TACTGTAAGG GGGATCCGCT GAAATAACAC ACTCACATGA CTCGGATCGT GAAATCCGAT GCCTCTTCGG CATTCAAGTG ATTACCCACT TTCTGCCCGG CACGCATTAC AACGCGATGC CACGCATTGC CGTGATGATG	CGAGGGGGG CGAGCGTGTC CCGATATGTT GATACTGTCC TCCGATCTTC GGGATCCGAA GGAATTCCTG TTATTGTAAA ATCCAGACTA ATGACATTCG GATCGAGGTC CCCACATCGT CATCGCCTTG TGCAATGGCT TGCAATGGCT TGCAAGGAGTC	GTTCATGCCA GTTCATGCCA CAACAAGGTC GCGATCCACG TTCATTCGTG TGCGCTCTTC ATGGATTCCG TTCCATTTCA TGCGATCCGC AACAAGCTGA GGCAAGATGG CCCAGGAATC GACCAAACTA TATGAAAGCC GACATTTCAG GACATTTCAG	GCTCATGCAA AGGGAGCCGG GGAAAACAGA TGGATTCTCT ACGCAATCCA GATTTCTGGA TTTTATGAAT AGCCTGCTCA GACCTGTTCA GAAATGGGAG TGCTGAACAG GAGTTCTCGC CATTCAGCTT AGGGAGATGC ACGGAGATGC	GATGTAGTTT AGCCCATGGA CACCACTTCT CTCAAATTCT CTTTCCGAAT TGAATCGCC GGATACGGAG AGGTTCCAAG ATGCCATTGA TTCAATCCAT GAATGTGAAG CAGACAAGAT CCAGTCAACT GCCGAATTAC	AAATGGAGCT ATATGGATGA TACTTCGAGG CGTTCGTTTT ATACCGAGGA TTCATTCATG TGAATCCATT CGCATACTTT AATCTCGATC GTCAAGAAAT TTGATGTCAC AATTATTTCG GCTCCAAGGG GCCCGTACCG TTCCCGAACA	GATGGCTCAT TCACCCATGA TCAACGGTCG GGGTAACTGG CCATCAAGGTGA CAACATGGTC CAACTGACGC TTCCCGGAAT TAAAGTTTGG CTGAGGTCGA CGTATCTTCT CTCCCGTGCT GTTTCCGCGG	CGAAGACCGC TTCGATCGTG CATCACCAAG CTGGAGAATC GATCTGGTTG CAATCCACAG TGTTCCTCTA AACAAGGAGG TGGAAAGCTC CCACACGGTG ACAAGCCGCC CCTACACGGA CATACCACTC ATACCACTC	•
	GCAGCCACGT	CAGTTCTGGG GGAGGAAATT	AGAAAGTGCT CAAAATGGAA	CAAGGAGGAG	GAGAGAGAGA	TTATGAGACT		ACAACTAC	GA



The sod-3 gene is located on chromosome X. Exemplary regulatory sequences include:

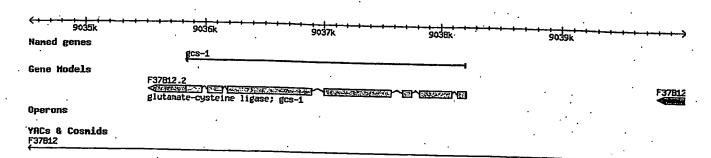
#### Exemplary sod-3 sequences:

#### Amino Acid Sequence

MLQSTARTAS KLVQPVAGVL AVRSKHTLPD LPFDYADLEP VISHEIMQLH HQKHHATYVN NLNQIEEKLH EAVSKGNLKE AIALQPALKF NGGGHINHSI FWTNLAKDGG EPSKELMDTI KRDFGSLDNL QKRLSDITIA VQGSGWGWLG YCKKDKILKI ATCANQDPLE GMVPLFGIDV WEHAYYLQYK NVRPDYVHAI WKIANWKNIS ERFANARQ

#### Spliced mRNA

CGTTTGCGGAGT
TCTCGCCGTC
CGCTCCAAGC
ACACTCTCC
AGATCTACTG
AGACATCT
TCAAAGCTT
TCATCAACCGG
ACCCTACCA
AGATCTCCC
AGATCTCCC
AGATCTCC
AGACATCTC
AGACATCTC
AGACATCTC
AATCAGATC
TCACGAGGCT
TCATCATCAA
AAGCATCATG
CCACCTACGT
TCAACGAGCT
TCATCATCAA
AAGCATCATG
ACCACTACC
CCACCTACGT
TCAACGATC
CCACCTACGT
TCAACGATC
CCACCTACGT
TCAACGATC
CCACCTACGT
TCAACGATC
CCACCTACGT
ATTCAATCAT
CCACCTGGATAA
CTTGCAAAAA
CCTCTTCTG
ACCACTACT
TCAAAGGAC
CCCTGGATAA
CTTGCAAAAA
CTTGCAAAAA
CTTTCTTCTG
ACATCACTAT
TCAAAGGAC
TCAAAGC
TCAAAGGAC
TCACCTTT
TCAAAGGAC
TCAAAGC
TCAAAGGAC
TCAAAGGAC
TCAAAGC
TCAAAGGAC
TCAAAGC
TCAAAGGAC
TCAAAGC
TCAAAAAATGT
CCGCCCAACT
TCAAAGGAC
TCCACCTT
TCAAAGGAC
TCCACTT
TCAAAGGAC
TCAAAAAATGT
TCCAAAGC
TCCCACTT
TCAAAGGAC
TCCACTT
TCAAAGGAC
TCACCT
TCAAAGC
TCCACTT
TCAAAGGAC
TCCACTT
TCAAAGGAC
TCCACTT
TCAAAGGAC
TCCACTT
TCAAAGGAC
TCCACT
TCAAAGGAC
TCCACT
TCAAAGGAC
TCCACT
TCAAAGC
TCCACT
TCAAAGGAC
TCCACT
TCAAAGGAC
TCCACT
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TCCACT
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TCCACT
TCAAAGGAC
TCCACT
TCAAAGC
TCCACT
TCAAAGC
TCCACT
TCAAAGC
TCCACT
TCCACCT
TCCACCT
TCCACT
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TCCACT
TCCACCT
TCCACT
TCCACT
TCCACT
TCCACCT
TCCACT
TCCACCT
TCCACCT
TCCACCT
TCCACCT



The gcs-1 gene is located on chromosome II. An exemplary regulatory sequence is:

#### Exemplary gcs-1 sequences:

## Amino Acid Sequence

MGLLTKGSPL TWAETVPHID YIKKHGIAQF INLYHRLKSR HGDQLKWGDE IEYTIVKFDD ANKKVRVSCK AEELLNKLQA
EEQVNAMLGT ANRFLWRPEF GSYMIEGTPG MPYGGLIACF NIVEANMKLR RQVVKKLLKK DETCLSISFP SLGVPGFTFP
EVAADRKNDD AANSVFWPEQ AVFLGHPRFK NLTKNIKGRR GSKVAINVPI FKDTNTPSPF VEDLSALGGP DDTRDAKPDH
IYMDHMGFGM GCCCLQVTFQ AVNVDEARWL YDQLTPITPI LLALSAATPI FRGKLSNVDS RWDIISASVD DRTPEERGLE
PLKNSKWVID KSRYDSTDCY IYPCSVGYND IPLQYDETIY KQLIDGNIDE PLAKHIAHMF IRDPHQVFRE RIEQDDEKSS
EHFETIQSSN WMNMRFKPPP PDAPEIGWRV EFRPTEVQLT DFENAAYCCF VVLLTRMMIS FRLTYLMPIS MVTENMKRAQ
QKDAVLNQKF LFRKGLAECK SAPENLKGSE KCGPPSQDIE EMSIDEIING KKNGFPGLIS LIRQFLDSAD VDVDTRCTIS
QYLNFISKRA TGEINTLAHW TRGFVQSHPA YKHDSDVNDN IVYDLLKKMD AISNGEDHCE KLLGCYRSKT DHAISAAVRK

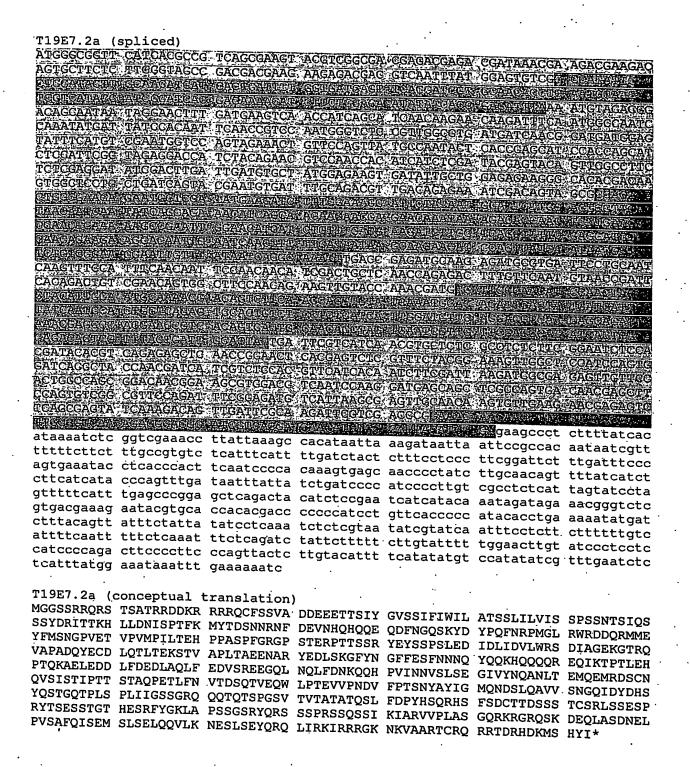
#### Spliced mRNA

tttgcagaAT GGGTCTTTTG ACGAAAGGTA GTCCGTTGAC GTGGGCAGAA ACCGTACCGC ACATTGATTA TATCAAGAAG TGAATACACT ATTGTAAAAT TTGATGACGC AAACAAGAAA GTTCGCGTGT CGTGCAAAGC TGAAGAGCTT CTTAATAAGT TACAAGCCGA AGAGCAGGTG AATGCGATGC TTGGAACTGC CAATCGATTC CTTTGGAGAC CAGAATTCGG ATCCTACATG ATCGAGGGAA CCCCCGGAAT GCCTTACGGA GGTCTCATCG CTTGCTTCAA CATTGTCGAG GCAAACATGA AATTGCGCAG ACAGGTCGTC AAAAAGTTAT TAAAGAAGGA TGAAACATGT CTATCGATAT CGTTCCCATC TCTTGGAGTA CCTGGATTCA CATTCCCGGA AGTAGCAGCT GATAGAAAGA ATGATGATGC AGCTAATAGC GTTTTCTGGC CAGAACAAGC TGTATTCTTG CAAGGATACG AACACCCCCA GTCCATTCGT TGAAGATTTA TCTGCACTTG GAGGTCCTGA TGATACTCGT GATGCGAAAC CTGATCACAT TTATATGGAT CATATGGGAT TCGGAATGGG GTGCTGTTGT CTTCAAGTCA CTTTCCAGGC TGTGAACGTC GATGAAGCCA GATGGTTGTA CGATCAGCTG ACACCGATTA CACCGATTCT ACTGGCACTC TCTGCCGCCA CACCAATCTT CCGTGGAAAA TTATCCAATG TCGATTCTAG ATGGGATATC ATTAGTGCAA GTGTCGACGA TCGTACACCG GAGGAAAGAG GATTGGAACC TCTCAAGAAT TCGAAATGGG TTATTGATAA GAGTCGCTAC GACTCCACGG ACTGTTACAT TTATCCATGT TCTGTTGGCT ACAATGATAT TCCTCTTCAA TACGACGAAA CCATATATAA ACAACTAATT GATGGAAATA TTGATGAGCC ACTGGCAAAA CATATTGCGC ATATGTTCAT TCGTGATCCA CATCAAGTTT TCCGTGAGCG TATCGAACAG GACGATGAGA AAAGCAGTGA ACACTTTGAA ACAATTCAAT CATCGAATTG GATGAACATG CGATTCAAGC CACCACCACC AGATGCTCCA GAAATCGGAT GGAGAGTCGA ATTCCGGCCA ACTGAAGTTC AACTGACCGA CTTTGAAAAT GCAGCATACT GTTGCTTCGT TGTATTGCTC ACCAGAATGA TGATCTCCTT CAGGCTGACA TATTTGATGC CAATTTCAAT GGTTACTGAA AATATGAAGC GTGCTCAGCA AAAAGATGCA GTTCTCAATC AGAAATTCCT GTTCAGAAAA GGATTGGCTG AGTGCAAATC TGCTCCCGAA AATTTGAAAG GATCGGAGAA ATGTGGACCA CCTAGTCAAG ATATTGAAGA AATGTCGATT GATGAGATTA TCAATGGAAA GAAAAATGGA TTCCCAGGTC TCATTTCACT TATTCGCCAA TTTCTAGATT CTGCTGATGT TGATGTGGAT ACTCGGTGTA CGATTTCTCA ATATTTGAAC TTTATTTCGA AACGAGCAAC TGGAGAGATT AATACTTTGG CTCACTGGAC ACGTGGATTC GTACAATCTC ATCCTGCATA CAAACATGAC AGTGATGTAA ATGATAATAT AGTTTACGAT CTTTTGAAAA AGATGGATGC CATCTCAAAC GGAGAAGATC ACTGTGAGAA GCTGCTCGGA TGCTACCGCT CTAAAACCGA TCATGCCATT TCTGCTGCTG TTCGCAAAGC TGAAGAGCAC ATGATCGTGT CCAGCCAAAA ACGTGCACAT TAGGCGataa ttgattgatt atgtgatttt aatttatta tgttctatac gtcgtgtttc ccattccttc taggccttcc atgattcaca atttttcgat gccatatcaa tttagttggc catctacatt aaattactga tatgttgatg ctattttcta gtaagcagat gtcagtgttt agtaattcaa aaatttaaac tetgaattte taaatgettg ttttttgagt agtaggaate agtacgaatg gtacattaat etgaaaataa tttcatattt atgtacaatg ctccctgaa tccatcatat aattattatc cgtgttg

```
T19E7.2c (spliced)
  aatcgttctt cttcttattt tctacagctg atgatgtttg atgaaggttt tattttcctt gctttttcca
  ccctgttaat attattttcg atattcccaa aaataattcc aaattttcag tccatattca tctggatact
  gatoggatoa ogacaaaaca tottotggao aatatatoao ogacatttag tgagtatgao ttgaaaagtg
 catctgatca cttttcgagc cgttttgtcg ctagggactt tttaatgaat cagatgtact tttcgaattt
catctgatca cttttcgagc cgttttgtcg ctagggactt tttaatgaat cagatgtact tttcgaattt
ttaaggaaa aagcagtagt tgcacttttg aaacttaaat taatacaa aactagata tatttca
gaaRtGTACA CGGACAGCAA TATACGACA TTTGATGAAA TTAACGATCA GGACAGCAA GGAGAGATT
TCAATCGCCA ACCAGATAT GGATTACCAC AATTCAACCG TCCATTGGT CTCCGTTGGG GTCATCATCA
ACGGATGATC CACTATTCA TGTCGAATGG TCCAGTACAA ACTGTGCT CTCCGTTGGG GTCATCATCA
ACGGATGATC CACTATTCA TGTCGAATGG TCCAGTACAA ACTGTGCAC ACTGATCA CACTACAC CACTACACAC CACTACAC CACTACACAC CACTACAC CACTACAC
  tttagagcaa aagcagtagt tgcacttttg aaacttaaat taatatacaa aactatgata tatattttca
 cctcttttat cacataaaat ctcggtcgaa accttattaa agccacataa ttaaagataa ttaattccgc
 cacaataatc gttttttct tctttgccgt gtctcatttc attttgatct actctttcct cccttcggat
 tetttgattt eccagtgaaa tacetcaece actteaatee ceacaaagtg ageaacecet atettgcaac
 agtittatca tetetteate atacceagti tgataattta ttatetgate eccateceet tgtegeetet
 cattagtate etagttttte atttgageee ggageteaga etacatetee gaateateat acaaatagat
 agaaacgggt ctcgtgacga aagaatacgt gcaccacacg accccccat cctgttcacc cccatacacc
 tgaaaaatat gatetttaca gttattteta ttatateete aaateteteg taatategta teaattteet
 cttctttttt gtcattttca atttttctca aatttctcag atctattctt tttcttgtat ttttggaact
 tgtatccctc ctccatcccc agact
 T19E7.2c (conceptual translation)
 MYTDSNNRNF DEVNHQHQQE QDFNGQSKYD YPQFNRPMGL RWRDDQRMME YFMSNGPVET VPVMPILTEH
 PPASPFGRGP STERPTTSSR YEYSSPSLED IDLIDVLWRS DIAGEKGTRQ VAPADQYECD LQTLTEKSTV
 APLTAEENAR YEDLSKGFYN GFFESFNNNQ YQQKHQQQQR EQIKTPTLEH PTQKAELEDD LFDEDLAQLF
 EDVSREEGQL NQLFDNKQQH PVINNVSLSE GIVYNQANLT EMQEMRDSCN QVSISTIPTT STAQPETLFN
 VTDSQTVEQW LPTEVVPNDV FPTSNYAYIG MQNDSLQAVV SNGQIDYDHS YQSTGQTPLS PLIIGSSGRQ
 QQTQTSPGSV TVTATATQSL FDPYHSQRHS FSDCTTDSSS TCSRLSSESP RYTSESSTGT HESRFYGKLA
 PSSG$RYQRS SSPRSSQSSI KIARVVPLAS GQRKRGRQSK DEQLASDNEL PVSAFQISEM SLSELQQVLK
 NESLSEYORO LIRKIRRRGK NKVAARTCRO RRTDRHDKMS HYI*
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T19E7.2b (spliced)	•
gaATGTCACT, TCCATCTGAT TTTGCCTCCT CTCTTCTGGC ATCCTCTAC	a sanda
CGCTCCAGCA GCTGTCAACT CTTTTGACGA ACAAGAAGAA GAATCCAAG CAAATGTTCA ATCAACAACA GGTGGATCAA CAGCCCAAG	ACCACCAACA CCACCAAGAO
CAPATETICA ATCACCACA GETGEATCAA CACGGGCATC ATCACCAAG TCTCGAGCAO TTTTGACAGA CRETTGGGARGARGARGARGA	A ACATACTIGAN CATGTACCTE
TCTCGAGCAD TITTGACAGA GRETTGCCARCATGCATC ATCACCAAG	A TUCATACIGES TATTCACGAG
TEARBOART DE PAPEAUME CATALATURA L'ALGAMENT DE PAPEAU	
CHECAACAGE TO A TO A CONTROL TO THE TOTAL TO A TABLE A CONTROL TO A TOTAL TO	CONTRACTOR OF THE PROPERTY CONTRACTOR OF THE PRO
AGTCACGAGT CTCGTTTCTA CGGAAAGTTG GCTGCATCCA GTGGATGAC CACGTTCATC ACAATCTTCG ATTAACATCT GCACGATCAC	A CG CAGAGAGAGECRACEGEA
CACGTTCATC ACAATCTTCG ATTAAGATCG CGAGAGGTGT TCCACTGGC ACGTCAATCC AAGGATGAGC AGCTGGCCAG TCACATCAC	C. TACUARCEN TEATEGICIE
ACGTCAATCC AAGGATGAGC AGCTGGCCAG TGACAACGAG CTTCCAGTG ATGTCATTAA GGGAGTTGCA ACAAGTCTTC AACAACAAC	T ACCIGATATE TO THE TOTAL TOTAL TO THE TOTAL TOTAL TO THE TOTAL TOTAL TO THE TOTAL TO
ATGTCATTAN GCGACTTGCA ACANGTGTTG AAGAACGAGA GTCTCAGCG GCAAGATTCG TCGACGCGCT AAGAACGAGA GTCTCAGCC	LOGGOCY COATGATTTOGEAG
GCAAGATTCG TCGACGCGCA ATCAME AGC TCTAME AGC	A CA A CA
gaage cetetttat cacataaaa agecacataa ttaaagataa ttaatteege cacaataata ettaatteege	t otomb
agccacataa ttaaagataa ttaattccgc cacaataatc gttttttc atttgatct actcttcct cccttcggat tctttgattt	t totttage
attitgatet actetiteet eestieggat tetitgatit eeeagtgaa eeacaaagtg ageaaceet atetigeac agittiates tetitgati	a taccton
ccacaaagtg agcaaccct atcttgcaac agttttatca tctcttcat ttatctgatc cccatccct tgtcgctct cattagtatc ctattattatca	c ataggarate
ttatctgatc cccatcccct tgtcgcctct cattagtatc ctagtttttctctacctacatctcc gaatcatcat acaaatagat agaaacgggt ctagt	C attraces tgataattta
ctacatctcc gaatcatcat acaaatagat agaaacgggt ctcgtgacgaccccccat cctgttcacc cccatacacc tgaaaaatat catattat	a aagaataati sa
accccccat cctgttcacc cccatacacc tgaaaaatat gatctttacaaatctctcg taatatcgta tcaatttcct cttcttttt gtactttac	a gttatttat
aaatctctcg taatatcgta tcaatttcct cttcttttt gtcattttcaatctattctt tttcttgtat ttttggaact tgtatcgta	a attitude
atctattett tttettgtat ttttggaact tgtateette etecateeee etettgtaca tttteatata tgteeatata tegtttgaat etecateeee	C agacttons to
ctcttgtaca ttttcatata tgtccatata tcgtttgaat ctctcattt	a agacticccc ttcccagtta
	ua
T19E7.2b (conceptual translation)	
MSLPSDFASS LLASSTITNT TNTAPAAVNS FDEOFFESKY TINKY OVER	N COOVERNMENT
DOLLDIVATE SNIALIGHON DSPONALOUS OLDANDES OF A	
ATATOSLEDP YHSORHSESD CTTDSSSTCS BLGGERDDY	~~~ .Z.D.OD 4.1 4.1
RSSQSSIKIA RVVPLASGOR KRGROSKDEO LASDNEI DVC A FOLGENOL	GOVIONOSO
KIRRRGKNKV AARTCRORRT DRHDKMSHYI *	S ELQQVLKNES LSEYQRQLIR



### Human Glycogen synthase kinase-3 beta (GSK-3 beta).

## Human Glycogen synthase kinase-3 alpha (GSK-3 alpha).

121 181 241 301 361 421	amback ark?	gsgggsggp gvvyqarlae lnlvleyvpe lvdpdtavlk aelllgqpif rtppeaialc	gagtsipppg trelvaikkv tvyrvarhft lcdfgsakql pgdsgvdqlv ssllevtpss	vklgrdsgkv lqdkrfknre kakltipily vrgepnvsyi eiikvlgtpt rlspleacab	ttvvatlgqg lqimrkldhc vkvymyqlfr csryyrapel reqiremnpn	persqevayt nivrlryffy slayihsqgv ifgatdytss
--	-------------	---	--	--	--	--

#### Mouse Glycogen synthase kinase-3 beta.

121 181 241 301	vigngsfgvv ekkdevylnl dikpqnllld wsagcvlael wtkvfrprtp	yqaklcdsge vldyvpetvy pdtavlklcd llgqpifpgd peaialcsrl	lvaikkvlqd rvarhysrak fgsakqlvrg sgvdqlveii leytptarlt	krfknrelqi qtlpviyvkl epnvsyicsr kvlgtptreq pleacahsff	mrkldhcniv ymyqlfrsla yyrapelifg iremnpnyte	yihsfgichr atdytssidv fkfpqikahp
30T	wtxvirprtp	pealaicsrl	levtptarlt	pleacahsff	delrdnnykl	nnardtnalf
361	nfttqelssn	pplatilipp	hariqaaasp	panataasdt	nagdrgqtnn	aasasasnst

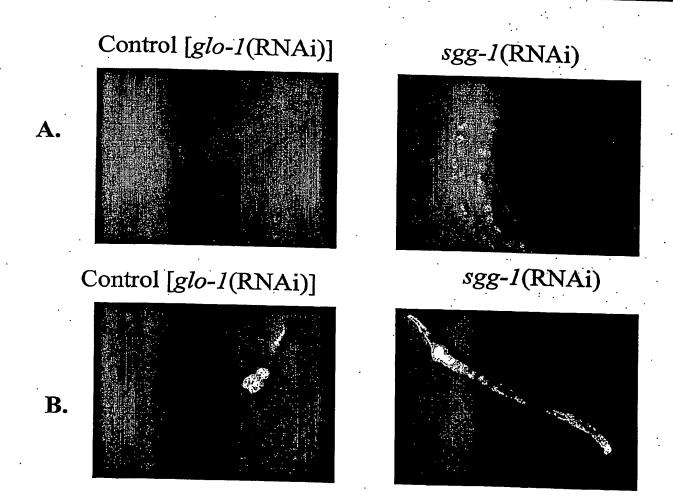
## Mouse Glycogen synthase kinase-3 alpha (GSK-3 alpha).

121	rkvttvvatv	qqdpersqev	asvwamgggv actdikvign	gasssgvggg	sggpgstsfl	1-1 1 11 61
181 241 301 361	yrelqimckl iiyvkvymyq ytssidvxsa	dhcnivrlqy lfrslayihs gcvlaellls vfksrtaprp	ffyssgekkd qgvchrdinl qpifpgdngv lhsalacwst	gsfgvvyqew dlylnlvley lvdpdtailk	ladtrelvai vpetvyxvar lcdfgsakql	kkvlqdkrfk

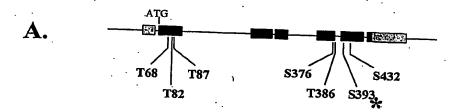
## GSK-3 [Caenorhabditis elegans].

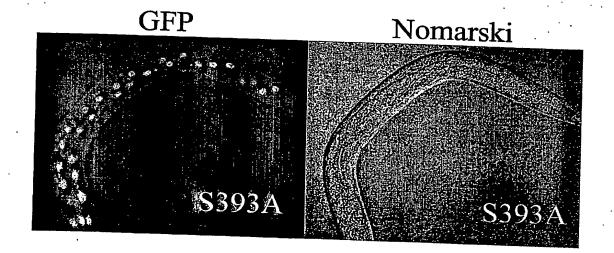
1	mnkqllscsl	ksgkqvtmvv	asvatdgvdg	qveisvvdak	vianasfava	flaklsttne
οт	<b>m</b> valkkvida	Kriknrelqi	mrklnhoniv	klkvffvssa	ekkdelulni	110:
121	TAGTHASVAT	ddiburiAAKI	VMVGLLrsla	vihsiaichr	diknomllid	manage 1 1-1 - 1
TOT	igsakyivin	epnvsylcsr	vvrapelifa	atnutneide	weagtamaol:	11
247	agvagiveii	vardfbflea	lasmnnnvke	fkfnaikahn	······································	
301	ieytptsrpt	pqaacqhaff	delrnpdarl	psgrplptle	mdanmataei	sptsgdvagp
361	sa ·		•	r-3-r-r-c	magping cger	apraguvagp

sgg-1 (GSK-3) inhibits constitutive SKN-1 nuclear accumulation and induction of its target gene gcs-1.

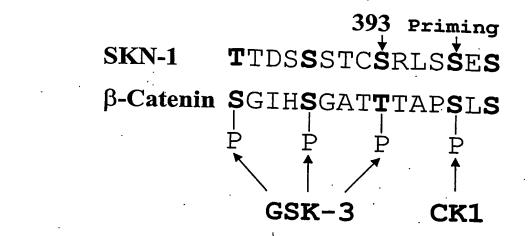


# Ala substitution at a predicted GSK-3 phosphorylation site results in nuclear localization of SKN-1





B.



Peptides: 1. WT

393 397

DCTTDSSSTCSRLSSESPRYTSE

2. WT+P397

DCTTDSSSTCSRLSSESPRYTSE \*

3. S393A+P397

DCTTDSSSTCARLSSESPRYTSE

Assay:

B.

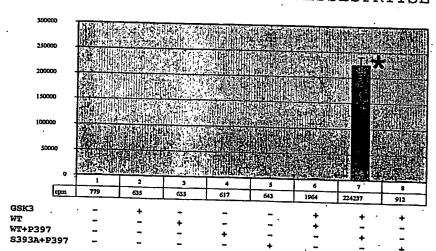


FIG. 39

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